

# Machines from Interlocking Molecules

**I**MAGINE a mechanical device created from a handful of molecules. Such a device could be a sensor that can detect infinitesimal traces of chemicals or biological agents, or it could be an on-off switch, a miniature building block for creating molecular computers. These ideas are moving closer to reality because of recent work on mechanically interlocking molecules at Livermore.

Unlike molecules that are joined by covalent bonds (by sharing pairs of electrons), mechanically interlocking molecules are physically joined, in the same way as the links in a chain or the rings in the Olympic Games symbol. Mechanically interlocking molecules are of growing interest to synthetic chemists, such as Livermore's Andrew Vance, who view them as potential building blocks for future molecular-scale devices—motors, sensors, and machines on the nanometer scale.

Vance heads up an effort originally funded through Laboratory Directed Research and Development to find new mechanically interlocking molecules that will consistently attach in a single layer on a gold surface. The team, which includes Vance, physicists Anthony Van Buuren and Art Nelson, and University of California at Davis physics graduate student Trevor Willey, is focusing on molecules known as catenanes and rotaxanes. A catenane has two or more interlocking rings. A rotaxane consists of a long, straight molecule—an “axle”—ringed by a doughnut-shaped molecule. Molecular “caps” at both ends of the rotaxane's axle keep the ring from sliding off. No chemical bond holds ring to ring or ring to axle.

Vance notes, “Interlocking molecules in solution are well understood, but not much is known about them on surfaces. Questions such as which molecules attach best, what's the best way to determine how well they're attached, and how to make the attachments stable are virtually unexplored.”

## Looping the Loop

The team started by exploring what kind of molecules worked best for forming a loop on a gold surface. Forming loops is the first step toward creating a monolayer of catenanes, in which

Chemist Andrew Vance working in his laboratory.

each attached loop would thread a ring. Vance explains, “We started at the most fundamental level, looking at how different molecules attached to the surface and how well they attached.” The challenge was to come up with a molecule that would consistently attach at not just one but both ends.

The team first tried a linear dithiol monomer. (A thiol is a molecule that has an atom of sulfur bound to an atom of hydrogen. This particular monomer had a thiol at each end; hence, it is a dithiol.) The monomer was, according to Vance, “a floppy molecule.” The researchers reasoned that when the sulfur atom at one end attached to the gold surface, the molecule would flop over and the sulfur at the other end would also attach, forming a loop. But measurements taken with x-ray absorption (XAS) and x-ray photoemission spectroscopy (XPS) at the Laboratory and at Stanford’s Synchrotron Radiation Laboratory revealed that only about 50 percent of the sulfur atoms had bonded to gold. (See the box, below right.) “In other words, most of the monomers had one unattached sulfur,” says Van Buuren.

Other measurements indicated that these monolayers were disordered and had molecules that, on average, were tilted slightly more than 55 degrees from the surface. “All these data indicated that most monomers were essentially standing on end on the surface,” notes Van Buuren. Because the concentration of monomers was quite high, the suspicion is that the monomers packed the surface, leaving little room for them to flop over and make a loop.

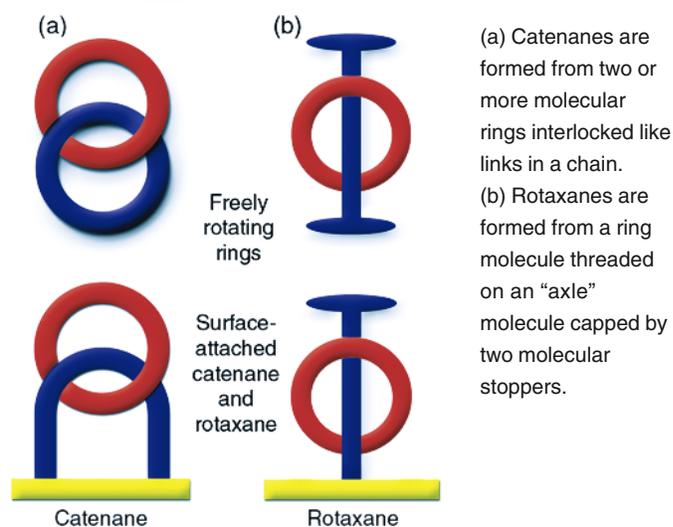
Another set of experiments used a polymer containing disulfide components. (A disulfide is two atoms of sulfur bound to each other.) In this case, the scientists expected the disulfide bonds to cleave, the sulfurs to bind to gold atoms, and the polymer to form a loop. XPS measurements showed that the resulting monolayer contained over 90 percent of bound sulfurs, evidence that nearly all the molecules had successfully formed surface-attached loops.

“The presence of a disulfide made it more likely that both sulfurs would attach to the surface,” says Vance. “All this pointed out the importance of designing molecules that will bind to surfaces in a predictable manner to form monolayers. In the case of surface-attached loops, simply preparing compounds with end components that bind well to the surface doesn’t guarantee loop formation. Other factors come into play, including the solution concentration and the shape of the molecule. Following these initial results, we also looked at molecules with built-in turns that encourage loop formation over single attachment.”

### Of Axles and Rings

Next, team members turned their attention to attaching rotaxanes to gold. As in the previous experiments, the team took two different approaches. One involved an electron-deficient, positively charged T-shaped thiol (which had the characteristic sulfur-hydrogen bond at one end and an anthracene stopper at the other) and an electron-rich crown ether ring. In solution, the two molecules are drawn to each other. The thiol threads the

crown ether to form a pseudorotaxane with only one stopper. “Our question was whether the pseudorotaxane would then attach to the gold, or would the crown ether ring slip off, leaving only a thiol to attach to the surface,” explains Vance. Vance also synthesized a [3]rotaxane composed of three molecules: two crown ether rings threaded by an anthracene-capped thiol with a disulfide bond in the middle. “From our work with loops, we felt



### X-Ray Vision

To “see” what was happening with the synthesized molecules and the gold surface, the physicists in Andrew Vance’s team used two techniques—x-ray absorption spectroscopy (XAS) and x-ray photoemission spectroscopy (XPS). Both techniques use x rays from the soft end of the spectrum (with wavelengths between those of ultraviolet light and harder, medical x rays). For the photoemission measurements, the team used the soft x rays created by a beamline at the Stanford Synchrotron Radiation Laboratory as well as a newly acquired Physical Electronics Quantum 2000 scanning XPS system here at Livermore.

The two techniques enable scientists to obtain detailed and specific information about the monolayers under scrutiny. According to physicist Trevor Willey, XPS measurements reveal the chemical composition of what’s on the surface as well as the nature of chemical bonds between the surface and the material. “We used XPS to determine whether the sulfur atom of the thiol was bound to gold or whether the thiol was just lying on the surface, essentially unattached,” he explains. Measurements with XAS revealed the orientation of the molecule. “With XAS, we could tell whether the thiol molecules were standing up, lying down, or leaning in some direction relative to the gold surface,” Willey says. “This also gave us information on how well ordered the layer was—that is, whether the attached molecules were packed together in ordered domains or leaning randomly every which way.”

confident that when the disulfide bonds cleaved, we'd get surface-attached rotaxanes," says Vance.

The team's physicists took spectra of powder samples of the crown ether rings, anthracene caps, and [3]rotaxane for reference as well as a spectrum of thiol attached to gold. When the experimental results were compared to these control spectra, the spectra from the [3]rotaxane experiments did indeed show surface-attached rotaxanes. However, the spectra from experiments with the pseudorotaxane precursor were identical to that of simple thiol on gold.

"The results confirmed that even though we'd set up a process for the thiol to thread the rings in solution, the rings came off before the sulfur could attach to the gold," says Vance. "For the [3]rotaxane, the rings were locked into place by the endcaps right up until the two sulfur atoms cleaved and adsorbed to the gold."

### Links to Future Possibilities

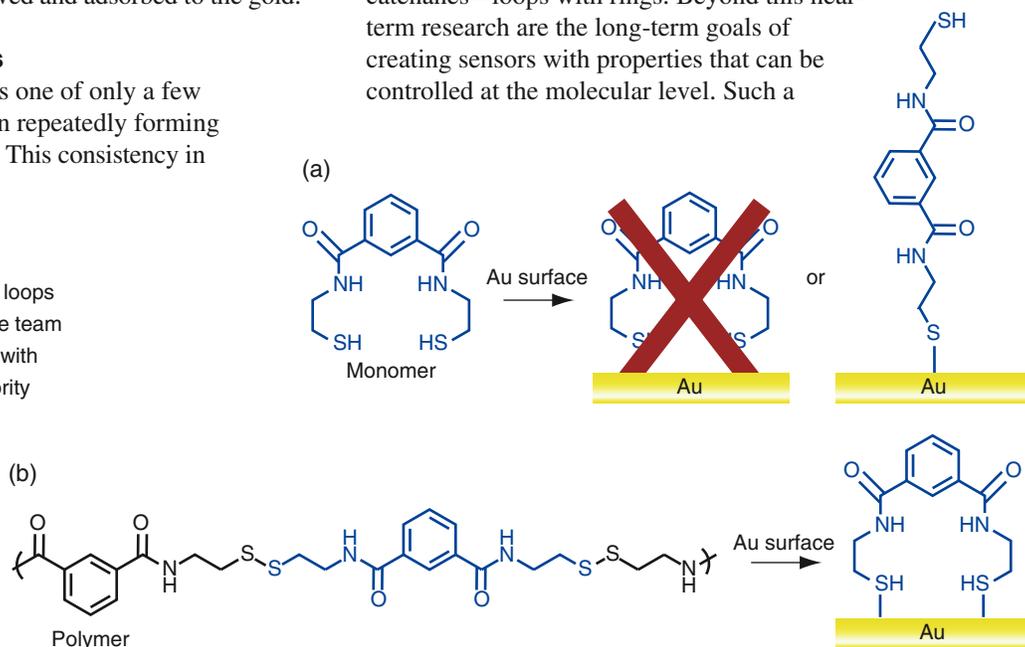
To date, the Livermore team is one of only a few groups that has been successful in repeatedly forming rotaxane monolayers on surfaces. This consistency in

results is important if such surface-attached molecules are to become molecular machines of the future.

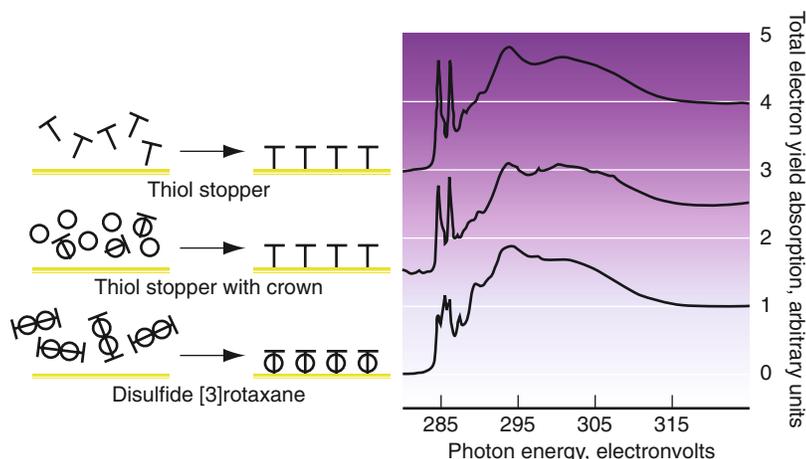
The success of Vance and his colleagues has led to a collaboration with a group from the University of California at Los Angeles (UCLA) led by chemistry professor and researcher Fraser Stoddart, one of the world's foremost experts in the synthesis of rotaxanes and catenanes. Vance's team has been taking interlocking molecules created by the UCLA group, attaching them to surfaces, and using XAS and XPS to examine the results.

In addition, the team continues its fundamental studies of surface attachment and is beginning to explore attaching molecules to other surfaces, including silicon. Furthermore, they are working on ways to create surface-attached catenanes—loops with rings. Beyond this near-term research are the long-term goals of creating sensors with properties that can be controlled at the molecular level. Such a

The team experimented with creating loops from different molecules. (a) When the team tried to attach monomers terminating with sulfur-hydrogen bonds, the vast majority attached at just one end instead of forming the hoped-for loop on gold. (b) A polymer with disulfide linkages was far more successful in attaching its sulfurs to the gold surface.



Results of surface-attached rotaxane research. Researchers started with thiols in solution (T-shaped molecules), attached them to gold, and used the resulting spectrum from x-ray absorption spectroscopy as a reference. Beginning with crown ether rings and anthracene-capped thiols in solution, researchers attempted to create pseudorotaxanes (single rings on axles capped at one end) and attach them to gold. The resulting spectrum was nearly identical to the reference, indicating that almost all the rings slipped off before the thiols attached. But using disulfide [3]rotaxane—two rings threaded on a thiol and restrained by anthracene endcaps—was effective in creating a surface-attached rotaxane. The resulting spectrum shows peaks similar to the reference spectrum for rotaxane powder.



sensor might have arrays of surface-attached catenanes with rotating rings that have tunable properties.

“By controlling the rotation of the ring, for instance, we can create an on-off switch,” Vance explains. “Suppose you could create a ring that has a small hydrophobic component. In the presence of a water molecule, it would spin one way; without water present, it would spin the other way. You could also create rings that are electrochemically or optically reactive and turn them on or off by changing the charge at the surface or by the presence or absence of light. Developing these switchable features is on our list of plans for the future.”

Vance believes the combination of synthetic chemistry and spectroscopy, chemists and physicists is a critical element in making this research possible. “What we’re doing now,” he continues, “is fundamental science that has intriguing possibilities. In the future, these surface-attached interlocking molecules could be used in molecular machines, sensors, and electronics in ways we’ve yet to even imagine.” It all comes down to being able to understand and control these small structures on the molecular and atomic level. And it’s a combination of chemistry and physics that, in the end, will make this possible.

—Ann Parker

**Key Words:** catenanes, molecular machines, rotaxanes, Stanford Synchrotron Radiation Laboratory, surface-attached mechanically interlocking molecules, x-ray absorption spectroscopy (XAS), x-ray photoemission spectroscopy (XPS).

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Members of the interlocking molecules research team. From left, Trevor Willey, Anthony Van Buuren, Cheryl Evans, and Art Nelson.

## An Idea Whose Time Has Come

Nearly a century ago, Richard Martin Willstätter, a German chemist destined to win a Nobel Prize in chemistry for synthesizing complex organic molecules, raised the possibility of interlocked molecular rings. It took until the early 1960s for synthetic chemists to invent procedures for forming such molecules in the laboratory.

One such method invoked brute statistics. Mix a huge number of ring-shaped molecules with U-shaped molecules inclined to form rings in solution, and by sheer statistical chance, the linear molecule will thread the circular molecule before forming a ring. The first catenane resulted from such a threading process.

Nowadays, synthetic chemists such as Livermore’s Andrew Vance use a method called template synthesis, which offers far more control over the synthesis of these structures. Template synthesis techniques use metal ions or noncovalent interactions such as hydrogen bonding, which force the stringlike molecules to thread the rings, providing a less hit-or-miss way to create catenanes and rotaxanes.

